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=> s trichothecene

L1 5456 TRICHOTHECENE

=> s l1 and (gastric motility)

L2 0 L1 AND (GASTRIC MOTILITY)

=> s l1 and (obesity or diet? or overeat? or satia? or (food intake))

L3 478 L1 AND (OBESITY OR DIET? OR OVEREAT? OR SATIA? OR (FOOD INTAKE))

=> s l3 and (DOn or (4 deoxynivalenol))

L4 66 L3 AND (DON OR (4 DEOXYNIVALENOL))

=> s l4 and P2x1 and (non desensitiz?) and agonist#

L5 0 L4 AND P2X1 AND (NON DESENSITIZ?) AND AGONIST#

=> s l4 and (P2x1 receptor)

L6 0 L4 AND (P2X1 RECEPTOR)

=> s l6 and oral?

L7 0 L6 AND ORAL?

=> s l5 and oral?

L8 0 L5 AND ORAL?

=> s l4 and oral?

L9 20 L4 AND ORAL?

=> d l9 1-20 ibib abs

L9 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:999884 CAPLUS

DOCUMENT NUMBER: 140:235011
TITLE: Deoxynivalenol-induced mitogen-activated protein kinase phosphorylation and IL-6 expression in mice suppressed by fish oil
AUTHOR(S): Moon, Yuseok; Pestka, James J.
CORPORATE SOURCE: Department of Food Science and Human Nutrition, Michigan State University, East Lansing, MI, 48824-1224, USA
SOURCE: Journal of Nutritional Biochemistry (2003), 14(12), 717-726
CODEN: JNBIEL; ISSN: 0955-2863
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **trichothecene** mycotoxin deoxynivalenol (DON) induces IgA hyper elevation and mesangial IgA deposition in mice that can mimic early stages of human IgA nephropathy (IgAN). Among potential mediators of this disease, interleukin-6 (IL-6) may play a particularly critical role in IgA elevation and disease exacerbation. Based on previous findings that **dietary** fish oil (FO) can suppress DON-induced IgAN, we hypothesized that FO may inhibit the induction of IL-6 expression by DON in vivo and in vitro. Mice were fed modified AIN 93G diet with 7% corn oil (CO) or with 1% corn oil plus 6% menhaden fish oil (FO) for up to 8 wk and then exposed acutely to DON by oral gavage. DON-induced blood plasma IL-6 and splenic mRNA elevation in FO-fed mice were suppressed after 8 wk compared to the CO-fed group. The effects of FO on phosphorylation of mitogen-activated protein kinases (MAPKs), critical upstream transducers of IL-6 up-regulation, were also assessed. DON-induced phosphorylation of extracellular signal regulated protein kinases 1 and 2 (ERK1/2) and c-Jun N-terminal kinases 1 and 2 (JNK1/2) was suppressed in the spleen of mice fed FO, whereas p38 was not. Splenic COX-2 mRNA expression, which enhances the DON-induced IL-6, was also decreased by FO, whereas blood plasma levels of the COX-2 metabolite PGE2 were not affected. To confirm the in vivo findings, the effects of pretreatment with the 2 main n-3 polyunsatd. fatty acids in FO, eicosapentaenoic acid (C20:5n-3; EPA) and docosahexaenoic acid, (C22:6n-3; DHA), on DON-induced IL-6 expression were assessed in LPS-treated RAW 264.7 macrophage cells. Consistent with the in vivo findings, both EPA and DHA suppressed IL-6 superinduction by DON and impaired the DON-induced ERK1/2 and JNK1/2 phosphorylation. The n-6 polyunsatd. arachidonic acid (C20:4n-3) had markedly less effects on these MAPKs. Thus, the capacity of FO and its component n-3 fatty acids to suppress IL-6 expression and ERK 1/2 and JNK 1/2 activation might help explain the reported suppressive effects of these lipids on DON-induced IgA nephropathy.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:581758 CAPLUS
DOCUMENT NUMBER: 132:165241
TITLE: Fusarium mycotoxins: a review of global implications for animal health, welfare and productivity
AUTHOR(S): D'Mello, J. P. F.; Placinta, C. M.; Macdonald, A. M. C.
CORPORATE SOURCE: Department of Biotechnology, The Scottish Agricultural College, Edinburgh, UK
SOURCE: Animal Feed Science and Technology (1999), 80(3-4), 183-205
CODEN: AFSTDH; ISSN: 0377-8401
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with many refs., is given on *Fusarium* mycotoxins that covers issues such as metabolism, syndromes, interactions, residues, tolerance limits and amelioration. Trichothecenes, zearalenone (ZEN) and fumonisins are the major *Fusarium* mycotoxins occurring on a worldwide basis in cereal grains, animal feeds and forages. Other important *Fusarium* mycotoxins include moniliformin and fusaric acid. Spontaneous outbreaks of *Fusarium* mycotoxicoses were recorded in Europe, Asia, New Zealand and South America and chronic exposure occurs on a regular and more widespread scale. The metabolism and adverse effects of the *Fusarium* mycotoxins are considered in this review with particular reference to recent data on specific and proposed syndromes and to interactions among co-occurring mycotoxins. Within the trichothecene group, deoxynivalenol (DON) is associated with emesis, feed refusal and depressed feed intake in pigs, while T-2 toxin and diacetoxyscirpenol (DAS) are now clearly linked with oral lesions in poultry. The gut microflora of farm livestock are able to transform DON to a de-epoxy derivative. But the ovine metabolism of ZEN gave five metabolites and relatively high levels of these forms may be excreted in the urine as glucuronides. There is now undisputed evidence that ZEN and its metabolites possess estrogenic activity in pigs, cattle and sheep, but T-2 toxin also was implicated in reproductive disorders in farm livestock. Fumonisins are pos. linked with pulmonary edema in pigs, leukoencephalomalacia in equines and with deranged sphingolipid metabolism in these animals. *Fusarium* mycotoxins also were provisionally implicated in ovine ill-thrift, acute mortality of poultry and in duodenitis/proximal jejunitis of horses. Several *Fusarium* mycotoxins may co-occur in a particular feed ingredient or in compound feeding stuffs. In general, combinations of *Fusarium* mycotoxins result in additive effects, but synergistic and/or potentiating interactions were observed and are of greater concern in livestock health and productivity. Synergistic effects were reported between DON and fusaric acid; DON and fumonisin B1 (FB1); and DAS and the *Aspergillus*-derived aflatoxins. Limited evidence of potentiation between FB1 and DON or T-2 toxin has also emerged recently. Additive and synergistic effects between known and unidentified mycotoxins may account for enhanced adverse effects observed on feeding *Fusarium*-contaminated diets. The potential for transmission of DON into eggs and of ZEN into porcine kidney and liver was demonstrated. However, lactational carry-over of FB1 appears not to occur, at least in cows and sows. Livestock health, welfare and productivity may be severely compromised by consumption of DON, T-2 toxin, DAS, ZEN and fumonisins and by interactions among these mycotoxins. Safety of some animal products may also be at risk. Also, in view of the limited options available for remediation, exploitation of crops resistant to *Fusarium* infection offers the most viable strategy for reducing mycotoxin contamination of grain and animal feed.

REFERENCE COUNT: 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:690714 CAPLUS

DOCUMENT NUMBER: 130:62269

TITLE: The effects of trichothecenes on host defense against infectious diseases

AUTHOR(S): Sugita-Konishi, Yoshiko; Hara-Kudo, Yukiko; Kasuga, Fumiko; Kumagai, Susumu

CORPORATE SOURCE: Dep. Biomed. Food Res., Natl. Inst. Infectious Diseases, Toyama, Shinjuku-ku, Tokyo, 162-8640, Japan

SOURCE: Maikotokishin (Tokyo) (1998), 47, 19-23

CODEN: MAIKD3; ISSN: 0285-1466

PUBLISHER: Maikotokishin Kenkyukai

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors studied the effect of relatively low doses of 5 trichothecenes (deoxynivalenol (DON), diacetoxysciperol (DAS), T-2 toxin (T-2), fusarenon-X (FX) and nivalenol (NIV)) on the host resistance against Salmonella infection using mice. Mice given daily each **trichothecene** in drinking water were infected **orally** with Salmonella enteritidis 14 days after the commencement of exposure to trichothecenes. It was found that **DON** was most effective among 5 **trichothecene** derivs. in decreasing the resistance against Salmonella infection. This effect of **DON** was associated with the reduction of serum anti-Salmonella IgM titer and delayed type hypersensitivity reaction, both of which are regarded as defense mechanisms against Salmonella infection. These results suggest that **dietary** exposure to low doses of **DON** enhances the susceptibility to **oral** infection to Salmonella through toxic effects on cellular and humoral immunity.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES-AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 20 USPATFULL on STN
 ACCESSION NUMBER: 2005:57290 USPATFULL
 TITLE: Method of treating and preventing cancer
 INVENTOR(S): Kaufmann, Doug A., Rockwall, TX, UNITED STATES

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2005049207 | A1 | 20050303 |
| APPLICATION INFO.: | US 2003-674145 | A1 | 20030929 (10) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2003-499976P | 20030903 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | Michael A. O'Neil, Michael A. O'Neil, P.C., Suite 820, 5949 Sherry Lane, Dallas, TX, 75225 | |
| NUMBER OF CLAIMS: | 62 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 1657 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention comprises a method of treating cancer. Specifically, the method involves administering one or more anti-fungal agents in amounts, at frequencies, and for durations which are effective in preventing and treating cancer. The method further comprises the administration of a low carbohydrate diet which may be used either in combination with the aforesaid anti-fungal agent or separately therefrom.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 5 OF 20 USPATFULL on STN
 ACCESSION NUMBER: 2004:133977 USPATFULL
 TITLE: Novel multi-ring organic compounds for regulating gut motility and food intake
 INVENTOR(S): Krantis, Anthony, Ontario, CANADA
 Durst, Tony, Ontario, CANADA

| | NUMBER | KIND | DATE |
|-----------------------|---|------|---------------|
| PATENT INFORMATION: | US 2004102514 | A1 | 20040527 |
| APPLICATION INFO.: | US 2003-250986 | A1 | 20031205 (10) |
| | WO 2002-CA25 | | 20020111 |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | Leon R Yankwich, Yankwich & Associates, 201 Broadway, | | |

Cambridge, MA, 02139

NUMBER OF CLAIMS: 30

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 27 Drawing Page(s)

LINE COUNT: 2424

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Multi-ring organic compounds useful in compositions and methods for regulating gut motility to modulate **food intake** and treat **obesity** and malnutrition are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 6 OF 20 USPATFULL on STN

ACCESSION NUMBER: 2000:57940 USPATFULL

TITLE: Tolerance of **trichothecene** mycotoxins in plants and animals through the modification of the peptidyl transferase gene

INVENTOR(S): Harris, Linda, Greely, Canada

Gleddie, Steve, Ottawa, Canada

PATENT ASSIGNEE(S): Her Majesty the Queen in right of ~~Canada~~, as represented by the Minister of Agriculture, ~~Canada~~ (non-U.S. government)
Agri-Food Canada, Canada (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 6060646 | | 20000509 |
| APPLICATION INFO.: | US 1997-909828 | | 19970812 (8) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Campell, Bruce R. | | |
| LEGAL REPRESENTATIVE: | Rothwell, Figg, Ernst & Kurz, P.C. | | |
| NUMBER OF CLAIMS: | 18 | | |
| EXEMPLARY CLAIM: | 1,9 | | |
| NUMBER OF DRAWINGS: | 6 Drawing Figure(s); 6 Drawing Page(s) | | |
| LINE COUNT: | 1172 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Fusarium graminearum is a plant pathogen, attacking a wide range of plant species including corn (ear and stalk rot), barley, and wheat (head blight). Fusarium epidemics result in millions of dollars of losses in crop revenues. Fusarium graminearum infection in the cereals reduces both grain yield and quality. Mycotoxins are produced by many fungal Fusarium species and thus the grain becomes contaminated with these mycotoxins, such as the trichothecenes. The major **trichothecene** produced by F. graminearum is deoxynivalenol (abbreviated as **DON**, also known as vomitoxin). Trichothecenes are potent protein synthesis inhibitors and are quite toxic to humans and livestock. A yeast gene has been identified which is resistant to the **trichothecene**, trichodermin. A corresponding plant gene has been prepared, which has been used to transform plants and would be suitable to transform animals. These transformed plants have an increased resistance to Fusarium infestation. Potentially, transformed animals could have an increased tolerance to the **trichothecene** mycotoxins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 7 OF 20 USPATFULL on STN

ACCESSION NUMBER: 95:31988 USPATFULL

TITLE: **Trichothecene** conjugates

INVENTOR(S): Theodore, Louis J., 622 152nd Pl., SW., Lynnwood, WA, United States 98037
Reno, John M., 2452 Elm Dr., Brier, WA, United States 98036

- Kasina, Sudhakar, 13710 115th Ave. NE., Kirkland, WA,
United States 98034
Sanderson, James A., 1539 NE. 103rd Ave., Seattle, WA,
United States 98125
- Abrams, Paul G., 2125 First Ave., #1602, Seattle, WA,
United States 98121

NUMBER KIND DATE

PATENT INFORMATION: US 5405966 19950411
APPLICATION INFO.: US 1993-73118 19930607 (8)
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-943184, filed
on 10 Sep 1992, now abandoned which is a continuation
of Ser. No. US 1988-194642, filed on 16 May 1988, now
patented, Pat. No. US 5157104, issued on 20 Oct 1992
which is a continuation-in-part of Ser. No. US
1985-788325, filed on 17 Oct 1985, now patented, Pat.
No. US 4744981, issued on 17 May 1988
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Fan, Jane T.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 1182

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Conjugates of trichothecenes and agents that bind to a defined
population of cells are disclosed. Preferred are conjugates of
trichothecene molecules with polyclonal or monoclonal antibodies
or fragments thereof that recognize antigens that are present only on
tumor cells or are augmented in their expression on tumor cells as
compared to normal tissues. **Trichothecene** molecules are
coupled to the agent through non-covalent and covalent linkages, such as
peptide bonds, disulfide bonds, thioester bonds, or thioether bonds. A
method for inhibiting the growth and metabolism of antigen-positive
cells is also disclosed. Derivatized **trichothecene** compounds
prepared for conjugation to targeting agents are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 8 OF 20 USPATFULL on STN
ACCESSION NUMBER: 92:87034 USPATFULL
TITLE: **Trichothecene** conjugates
INVENTOR(S): Sivam, Gowsala, Edmonds, WA, United States
Abrams, Paul G., Seattle, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S.
corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5157104 19921020
APPLICATION INFO.: US 1988-194642 19880516 (7)
DISCLAIMER DATE: 20050517
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1985-788325, filed
on 17 Oct 1985, now patented, Pat. No. US 4744981,
issued on 17 May 1988
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Cashion, Jr., Merrell C.
ASSISTANT EXAMINER: Rozycki, Andrew G.
LEGAL REPRESENTATIVE: Seed and Berry
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1,2
LINE COUNT: 547

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Conjugates of trichothecenes and agents that bind to a defined population of cells are disclosed. Preferred are conjugates of **trichothecene** molecules with polyclonal or monoclonal antibodies or fragments thereof that recognize antigens that are present only on tumor cells or are augmented in their expression on tumor cells as compared to normal tissues. **Trichothecene** molecules are coupled to the agent through non-covalent and covalent linkages, such as peptide bonds, disulfide bonds, thioester bonds, or thioether bonds. A method for inhibiting the growth and metabolism of antigen-positive cells is also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 9 OF 20 USPATFULL on STN
ACCESSION NUMBER: 90:17501 USPATFULL
TITLE: **Trichothecene** conjugates and methods of use
INVENTOR(S): Sivam, Gowsala, Edmonds, WA, United States
PATENT ASSIGNEE(S): Neorx Corporation, Seattle, WA, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 4906452 | | 19900306 |
| APPLICATION INFO.: | US 1988-187113 | | 19880428 (7) |
| DISCLAIMER DATE: | 20050517 | | |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 1985-788325, filed on 17 Oct 1985, now patented, Pat. No. US 4744981, issued on 17 May 1988 | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | - Granted | | |
| PRIMARY EXAMINER: | Rosen, Sam | | |
| LEGAL REPRESENTATIVE: | Leith, Debra | | |
| NUMBER OF CLAIMS: | 7 | | |
| EXEMPLARY CLAIM: | - 1,6 | | |
| LINE COUNT: | - 536 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Conjugates of trichothecenes and agents that bind to a defined population of cells are disclosed. Preferred are conjugates of **trichothecene** molecules with polyclonal or monoclonal antibodies or fragments thereof that recognize antigens that are present only on tumor cells or are augmented in their expression on tumor cells as compared to normal tissues. **Trichothecene** molecules are coupled to the agent through non-covalent and covalent linkages, such as peptide bonds, disulfide bonds, thioester bonds, or thioether bonds. Methods for reducing intoxicification in a recipient of a **trichothecene** and an agent and for producing a **trichothecene** conjugate with improved solubility are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 10 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2003608631 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14690764
TITLE: Deoxynivalenol-induced mitogen-activated protein kinase phosphorylation and IL-6 expression in mice suppressed by fish oil.
AUTHOR: Moon Yuseok; Pestka James J
CORPORATE SOURCE: Department of Food Science and Human Nutrition, Michigan State University, East Lansing, MI 48824-1224, USA.
CONTRACT NUMBER: DK058833 (NIDDK)
ES 09521 (NIEHS)

SOURCE: Journal of nutritional biochemistry, (2003 Dec) 14 (12)
717-26.
Journal code: 9010081. ISSN: 0955-2863.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20031224
Last Updated on STN: 20040723
Entered Medline: 20040722

AB The **trichothecene** mycotoxin deoxynivalenol (**DON**) induces IgA hyperlevelation and mesangial IgA deposition in mice that mimics the early stages of human IgA nephropathy (IgAN). Among potential mediators of this disease, interleukin-6 (IL-6) is likely to play a particularly critical role in IgA elevation and disease exacerbation. Based on previous findings that **dietary** fish oil (FO) suppresses **DON**-induced IgAN, we hypothesized that FO inhibits the induction of IL-6 expression by this mycotoxin in vivo and in vitro. Mice were fed modified AIN 93G **diet** amended with 7% corn oil (CO) or with 1% corn oil plus 6% menhaden fish oil (FO) for up to 8 weeks and then exposed acutely to **DON** by oral gavage. **DON**-induced plasma IL-6 and splenic mRNA elevation in FO-fed mice were significantly suppressed after 8 weeks when compared to the CO-fed group. The effects of FO on phosphorylation of mitogen-activated protein kinases (MAPKs), critical upstream transducers of IL-6 up-regulation, were also assessed. **DON**-induced phosphorylation of extracellular signal regulated protein kinases 1 and 2 (ERK1/2) and c-Jun N-terminal kinases 1 and 2 (JNK1/2) was significantly suppressed in spleens of mice fed with FO, whereas p38 was not. Splenic COX-2 mRNA expression, which has been previously shown to enhance **DON**-induced IL-6, was also significantly decreased by FO, whereas plasma levels of the COX-2 metabolite, prostaglandin E2, were not affected. To confirm in vivo findings, the effects of pretreatment with the two primary n-3 PUFAs in FO, eicosapentaenoic acid (20:5[n-3]; EPA) and docosahexaenoic acid, (22:6[n-3]; DHA), on **DON**-induced IL-6 expression were assessed in LPS-treated RAW 264.7 macrophage cells. Consistent with the in vivo findings, both EPA and DHA significantly suppressed IL-6 superinduction by **DON**, as well as impaired **DON**-induced ERK1/2 and JNK1/2 phosphorylation. In contrast, the n-6 PUFA arachidonic acid (20:4[n-3]) had markedly less effects on these MAPKs. Taken together, the capacity of FO and its component n-3 PUFAs to suppress IL-6 expression as well as ERK 1/2 and JNK 1/2 activation might explain, in part, the reported suppressive effects of these lipids on **DON**-induced IgA nephropathy.

L9 ANSWER 11 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:94382 BIOSIS
DOCUMENT NUMBER: PREV200400094271
TITLE: Deoxynivalenol-induced mitogen-activated protein kinase phosphorylation and IL-6 expression in mice suppressed by fish oil.
AUTHOR(S): Moon, Yuseok; Pestka, James J. [Reprint Author]
CORPORATE SOURCE: Department of Food Science and Human Nutrition, Michigan State University, East Lansing, MI, 48824-1224, USA
pestka@msu.edu
SOURCE: Journal of Nutritional Biochemistry, (December 2003) Vol. 14, No. 12, pp. 717-726. print.
CODEN: JNBIEL. ISSN: 0955-2863.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Feb 2004

Last Updated on STN: 11 Feb 2004

AB The **trichothecene** mycotoxin deoxynivalenol (**DON**) induces IgA hyper-elevation and mesangial IgA deposition in mice that mimics the early stages of human IgA nephropathy (IgAN). Among potential mediators of this disease, interleukin-6 (IL-6) is likely to play a particularly critical role in IgA elevation and disease exacerbation. Based on previous findings that **dietary** fish oil (FO) suppresses **DON**-induced IgAN, we hypothesized that FO inhibits the induction of IL-6 expression by this mycotoxin in vivo and in vitro. Mice were fed modified AIN 93G diet amended with 7% corn oil (CO) or with 1% corn oil plus 6% menhaden fish oil (FO) for up to 8 weeks and then exposed acutely to **DON** by oral gavage. **DON**-induced plasma IL-6 and splenic mRNA elevation in FO-fed mice were significantly suppressed after 8 weeks when compared to the CO-fed group. The effects of FO on phosphorylation of mitogen-activated protein kinases (MAPKs), critical upstream transducers of IL-6 up-regulation, were also assessed. **DON**-induced phosphorylation of extracellular signal regulated protein kinases 1 and 2 (ERK1/2) and c-Jun N-terminal kinases 1 and 2 (JNK1/2) was significantly suppressed in spleens of mice fed with FO, whereas p38 was not. Splenic COX-2 mRNA expression, which has been previously shown to enhance **DON**-induced IL-6, was also significantly decreased by FO, whereas plasma levels of the COX-2 metabolite, prostaglandin E2, were not affected. To confirm in vivo findings, the effects of pretreatment with the two primary n-3 PUFAs in FO, eicosapentaenoic acid (20:5(n-3); EPA) and docosahexaenoic acid, (22:6(n-3); DHA), on **DON**-induced IL-6 expression were assessed in LPS-treated RAW 264.7 macrophage cells. Consistent with the in vivo findings, both EPA and DHA significantly suppressed IL-6 superinduction by **DON**, as well as impaired **DON**-induced ERK1/2 and JNK1/2 phosphorylation. In contrast, the n-6 PUFA arachidonic acid (20:4(n-3)) had markedly less effects on these MAPKs. Taken together, the capacity of FO and its component n-3 PUFAs to suppress IL-6 expression as well as ERK 1/2 and JNK 1/2 activation might explain, in part, the reported suppressive effects of these lipids on **DON**-induced IgA nephropathy.

L9 ANSWER 12 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:494316 BIOSIS
DOCUMENT NUMBER: PREV199900494316
TITLE: Fusarium mycotoxins: A review of global implications for animal health, welfare and productivity.
AUTHOR(S): D'Mello, J. P. F. [Reprint author]; Placinta, C. M.; Macdonald, A. M. C.
CORPORATE SOURCE: Department of Biotechnology, Scottish Agricultural College, West Mains Road, Edinburgh, EH9 3JG, UK
SOURCE: Animal Feed Science and Technology, (Aug. 30, 1999) Vol. 80, No. 3-4, pp. 183-205. print.
CODEN: AFSTDH. ISSN: 0377-8401.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 1999
Last Updated on STN: 16 Nov 1999

AB Trichothecenes, zearalenone (ZEN) and fumonisins are the major Fusarium mycotoxins occurring on a worldwide basis in cereal grains, animal feeds and forages. Other important Fusarium mycotoxins include moniliformin and fusaric acid. Spontaneous outbreaks of Fusarium mycotoxicoses have been recorded in Europe, Asia, New Zealand and South America and, in addition, chronic exposure occurs on a regular and more widespread scale. The metabolism and adverse effects of the Fusarium mycotoxins are considered in this review with particular reference to recent data on specific and proposed syndromes and to interactions among co-occurring mycotoxins.

Within the **trichothecene** group, deoxynivalenol (**DON**) is associated with emesis, feed refusal and depressed feed intake in pigs, while T-2 toxin and diacetoxyscirpenol (**DAS**) are now clearly linked with oral lesions in poultry. The gut microflora of farm livestock are able to transform **DON** to a de-epoxy derivative. In contrast, the ovine metabolism of **ZEN** results in the production of five metabolites and relatively high levels of these forms may be excreted in the urine as glucuronides. There is now undisputed evidence that **ZEN** and its metabolites possess estrogenic activity in pigs, cattle and sheep, but T-2 toxin has also been implicated in reproductive disorders in farm livestock. Fumonisin is positively linked with pulmonary edema in pigs, leukoencephalomalacia in equines and with deranged sphingolipid metabolism in these animals. Fusarium mycotoxins have also been provisionally implicated in ovine ill-thrift, acute mortality of poultry and in duodenitis/proximal jejunitis of horses. Several Fusarium mycotoxins may co-occur in a particular feed ingredient or in compound feeding stuffs. In general, combinations of Fusarium mycotoxins result in additive effects, but synergistic and/or potentiating interactions have been observed and are of greater concern in livestock health and productivity. Synergistic effects have been reported between **DON** and fusaric acid, **DON** and fumonisin B1 (**FB1**); and **DAS** and the Aspergillus-derived aflatoxins. Limited evidence of potentiation between **FB1** and **DON** or T-2 toxin has also emerged recently. Additive and synergistic effects between known and unidentified mycotoxins may account for enhanced adverse effects observed on feeding Fusarium-contaminated diets. The potential for transmission of **DON** into eggs and of **ZEN** into porcine kidney and liver has been demonstrated. However, lactational carry-over of **FB1** appears not to occur, at least in cows and sows. It is concluded that livestock health, welfare and productivity may be severely compromised by consumption of **DON**, T-2 toxin, **DAS**, **ZEN** and fumonisins and by interactions among these mycotoxins. Safety of some animal products may also be at risk. Furthermore, in view of the limited options available for remediation, it is concluded that exploitation of crops resistant to Fusarium infection offers the most viable strategy for reducing mycotoxin contamination of grain and animal feed.

L9 ANSWER 13 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 2004006762 EMBASE
TITLE: Deoxynivalenol-induced mitogen-activated protein kinase phosphorylation and IL-6 expression in mice suppressed by fish oil.
AUTHOR: Moon Y.; Pestka J.J.
CORPORATE SOURCE: J.J. Pestka, Dept. of Food Sci. and Hum. Nutr., Michigan State University, East Lansing, MI 48824-1224, United States. pestka@msu.edu
SOURCE: Journal of Nutritional Biochemistry, (2003) Vol. 14, No. 12, pp. 717-726.
Refs: 77
ISSN: 0955-2863 CODEN: JNBIEL
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040116
Last Updated on STN: 20040116

AB The **trichothecene** mycotoxin deoxynivalenol (**DON**) induces IgA hyperlevelation and mesangial IgA deposition in mice that mimics the early stages of human IgA nephropathy (IgAN). Among potential mediators of this disease, interleukin-6 (IL-6) is likely to play a particularly critical role in IgA elevation and disease exacerbation. Based on previous findings that dietary fish oil (FO) suppresses

DON-induced IgA, we hypothesized that FO inhibits the induction of IL-6 expression by this mycotoxin in vivo and in vitro. Mice were fed modified AIN 93G diet amended with 7% corn oil (CO) or with 1% corn oil plus 6% menhaden fish oil (FO) for up to 8 weeks and then exposed acutely to DON by oral gavage. DON-induced plasma IL-6 and splenic mRNA elevation in FO-fed mice were significantly suppressed after 8 weeks when compared to the CO-fed group. The effects of FO on phosphorylation of mitogen-activated protein kinases (MAPKs), critical upstream-transducers of IL-6 up-regulation, were also assessed. DON-induced phosphorylation of extracellular signal regulated protein kinases 1 and 2 (ERK1/2) and c-Jun N-terminal kinases 1 and 2 (JNK1/2) was significantly suppressed in spleens of mice fed with FO, whereas p38 was not. Splenic COX-2 mRNA expression, which has been previously shown to enhance DON-induced IL-6, was also significantly decreased by FO, whereas plasma levels of the COX-2 metabolite, prostaglandin E(2), were not affected. To confirm in vivo findings, the effects of pretreatment with the two primary n-3 PUFAs in FO, eicosapentaenoic acid (20:5[n-3]; EPA) and docosahexaenoic acid, (22:6[n-3]; DHA), on DON-induced IL-6 expression were assessed in LPS-treated RAW 264.7 macrophage cells. Consistent with the in vivo findings, both EPA and DHA significantly suppressed IL-6 superinduction by DON, as well as impaired DON-induced ERK1/2 and JNK1/2 phosphorylation. In contrast, the n-6 PUFA arachidonic acid (20:4[n-3]) had markedly less effects on these MAPKs. Taken together, the capacity of FO and its component n-3 PUFAs to suppress IL-6 expression as well as ERK 1/2 and JNK 1/2 activation might explain, in part, the reported suppressive effects of these lipids on DON-induced IgA nephropathy. COPYRIGHT. 2003 Elsevier Inc. All rights reserved.

L9 ANSWER 14 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:243714 SCISEARCH

THE GENUINE ARTICLE: 899NW

TITLE: Truncated deoxynivalenol-induced splenic immediate early gene response in mice consuming (n-3) polyunsaturated fatty acids

AUTHOR: Kinser S; Li M X; Jia Q S; Pestka J J (Reprint)

CORPORATE SOURCE: Michigan State Univ, Dept Food Sci & Human Nutr, E Lansing, MI 48824 USA (Reprint); Michigan State Univ, Ctr Integrat Toxicol, E Lansing, MI 48824 USA; Michigan State Univ, Dept Microbiol & Mol Genet, E Lansing, MI 48824 USA

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF NUTRITIONAL BIOCHEMISTRY, (FEB 2005) Vol. 16, No. 2, pp. 88-95.

Publisher: ELSEVIER SCIENCE INC, 360 PARK AVE SOUTH, NEW YORK, NY 10010-1710 USA.

ISSN: 0955-2863.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 40

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Expression profiling has previously revealed that acute exposure to the common foodborne mycotoxin deoxynivalenol (DON) induces a large number of immediate early genes in murine lymphoid tissues that potentially affect immune function. The purpose of this study was to test the hypothesis that consumption of (n-3) polyunsaturated fatty acids (PUFAs) found in fish oil interferes with DON-induced immediate early gene expression. Mice were fed AIN-93G diet containing 1% corn oil (CO) plus 6% oleic acid (control) or a diet containing 1% CO, 2% fish oil enriched in the (n-3)-PUFAs docosahexaenoic and eicosapentaenoic acid and 4% oleic acid. After 12 weeks, the mice were gavaged orally with 25 mg/kg DON and the kinetics of immediate early gene expression in spleen monitored over 8 h by real-time

polymerase chain reaction (PCR). Deoxynivalenol was found to readily induce expression of cytokines (IL-1alpha, IL-1beta, and IL-6 and IL-11), chemokines (MCP-1, MCP-3, CINC-1 and MIP-2), components of the activator protein-1 (AP-1) transcription factor complex (c-Fos, Fra-2, c-Jun and JunB), as well as two hydrolases (MKP1, CnAbeta). Expression of these genes was transient, peaking within 2-4 h and declining thereafter, with the single exception being IL-11 that was elevated at 8 h. (n-3)-PUFA consumption significantly suppressed DON-induced expression of IL-1alpha, IL-6, IL-11, MCP-1, MCP-3, MIP-2 and Fra-2 at 8 h. In contrast, mice fed (n-3)-PUFA exhibited significant increases in MKP1 and CnAbeta expression. Taken together, these data suggest that dietary supplementation with (n-3)-PUFAs prematurely truncated cytokine, chemokine and transcription factor expression responses to DON that may impact its previously described capacity to disrupt immune function including immunoglobulin A (IgA) production. Since expression of many of these genes has been linked to mitogen-activated protein kinase (MAPK) activation, enhanced expression of MKP1, a negative MAPK regulator in (n-3)-PUFA-fed mice might contribute to this suppression. (C) 2005 Published by Elsevier Inc.

L9 ANSWER 15 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:42425 SCISEARCH

THE GENUINE ARTICLE: 879LY

TITLE: Docosahexaenoic acid attenuates mycotoxin-induced immunoglobulin a nephropathy, interleukin-6 transcription, and mitogen-activated protein kinase phosphorylation in mice

AUTHOR: Jia Q S; Zhou H R; Bennink M; Pestka J J (Reprint)

CORPORATE SOURCE: Michigan State Univ, Dept Food Sci & Human Nutr, E Lansing, MI 48823 USA (Reprint); Michigan State Univ, Ctr Integrat Toxicol, E Lansing, MI 48823 USA; Michigan State Univ, Dept Microbiol & Mol Genet, E Lansing, MI 48823 USA

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF NUTRITION, (DEC 2004) Vol. 134, No. 12, pp. 3343-3349.

Publisher: AMER INST NUTRITION, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.

ISSN: 0022-3166.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 66

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The purpose of this investigation was to evaluate the dose-dependent effects of docosahexaenoic acid (DHA) on deoxynivalenol (DON)-induced IgA nephropathy in mice and their relation to proinflammatory gene expression and mitogen-activated protein kinase (MAPK) activation. Consumption of a modified AIN-93G diet containing 1, 5, and 30 g/kg DHA resulted in dose-dependent increases of DHA in liver phospholipids with concomitant decreases in arachidonic acid compared with control diets. DHA dose dependently inhibited increases in serum IgA and IgA immune complexes (IC) as well as IgA deposition in the kidney in DON-fed mice; the 30 g/kg DHA diet had the earliest detectable effects and maximal efficacy. Both splenic interleukin-6 (IL-6) mRNA and heterogeneous nuclear RNA (hnRNA), an indicator of IL-6 transcription, were significantly reduced in DON-fed mice that consumed 5 and 30 g/kg DHA; a similar reduction was observed for cyclooxygenase (COX-2) mRNA. In a subsequent study, acute DON exposure (25 mg/kg body weight) induced splenic IL-6 mRNA and hnRNA as well as COX-2 mRNA in mice fed the control diet, whereas induction of both RNA species was significantly inhibited in mice fed 30 g/kg DHA. These latter inhibitory effects corresponded to a reduction in DON-induced phosphorylation of p38, extracellular-signal related

kinase 1/2, and c-Jun N-terminal kinase 1/2 MAPKs in the spleen. Taken together, the results indicate that DHA dose-dependently inhibited DON-induced IgA dysregulation and nephropathy, and that impairment of MAPK activation and expression of COX-2 and IL-6 are potential critical upstream mechanisms.

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ACCESSION NUMBER: 2004:557459 SCISEARCH

THE GENUINE ARTICLE: 827IN

TITLE: Docosahexaenoic acid and eicosapentaenoic acid, but not alpha-linolenic acid, suppress deoxynivalenol-induced experimental IgA nephropathy in mice

AUTHOR: Jia Q S; Shi Y H; Bennink M B; Pestka J J (Reprint)

CORPORATE SOURCE: Michigan State Univ, Dept Food Sci & Human Nutr, E Lansing, MI 48824 USA (Reprint); Michigan State Univ, Dept Microbiol & Mol Genet, E Lansing, MI 48824 USA; Michigan State Univ, Ctr Integrat Toxicol, E Lansing, MI 48824 USA

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF NUTRITION, (JUN 2004) Vol. 134, No. 6, pp. 1353-1361.

Publisher: AMER INST NUTRITION, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.

ISSN: 0022-3166.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 67

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Diets enriched in the (n-3) PUFAs, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and their precursor a-linolenic acid (ALA), were evaluated for efficacy in ameliorating the development of IgA nephropathy (IgAN) induced in mice by the mycotoxin deoxynivalenol (DON). The effects of DON were compared in mice that were fed for 18 wk with AIN-93G diets containing 1) 10 g/kg corn oil plus 60 g/kg oleic acid (control); 2) 10 g/kg corn oil plus 35 g/kg oleic acid and 25 g/kg DHA-enriched fish oil (DHA); 3) 10 g/kg corn oil plus 33 g/kg oleic acid and 27 g/kg EPA-enriched fish oil (EPA); and 4) 10 g/kg corn oil plus 37 g/kg oleic acid and 23 g/kg DHA + EPA (1:1) enriched fish oil (DHA + EPA). The DHA, EPA and DHA + EPA diets attenuated induction by dietary DON (10 mg/kg) of serum IgA and IgA immune complexes, kidney mesangial IgA deposition, and ex vivo IgA secretion by spleen cells. Consumption of the DHA + EPA diet for 8 wk significantly abrogated the DON-induced gene expression of interleukin (IL)-6, a requisite cytokine for DON-induced IgA nephropathy, in spleen and Peyer's patches. Finally, incorporation of ALA-containing flaxseed oil up to 60 g/kg in the AIN-93G diet did not affect DON-induced IgA dysregulation in mice. Taken together, both DHA and EPA, but not ALA, ameliorated the early stages of IgAN, and these effects might be related to a reduced capacity for IL-6 production.

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ACCESSION NUMBER: 2004:39516 SCISEARCH

THE GENUINE ARTICLE: 757ML

TITLE: Deoxynivalenol-induced mitogen-activated protein kinase phosphorylation and IL-6 expression in mice suppressed by fish oil

AUTHOR: Moon Y; Pestka J J (Reprint)

CORPORATE SOURCE: Michigan State Univ, Dept Food Sci & Human Nutr, E Lansing, MI 48824 USA (Reprint); Michigan State Univ, Inst Environm Toxicol, E Lansing, MI 48824 USA; Michigan State Univ, Dept Microbiol & Mol Genet, E Lansing, MI 48824 USA

COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF NUTRITIONAL BIOCHEMISTRY, (DEC 2003) Vol. 14,
No. 12, pp. 717-726.
Publisher: ELSEVIER SCIENCE INC, 360 PARK AVE SOUTH, NEW
YORK, NY 10010-1710 USA.
ISSN: 0955-2863.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 77

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The **trichothecene** mycotoxin deoxynivalenol (DON) induces IgA hyperlevelation and mesangial IgA deposition in mice that mimics the early stages of human IgA nephropathy (IgAN). Among potential mediators of this disease, interleukin-6 (IL-6) is likely to play a particularly critical role in IgA elevation and disease exacerbation. Based on previous findings that **dietary** fish oil (FO) suppresses DON-induced IgAN, we hypothesized that FO inhibits the induction of IL-6 expression by this mycotoxin in vivo and in vitro. Mice were fed modified AIN 93G diet amended with 7% corn oil (CO) or ~~with 1% corn oil plus 6% menhaden fish oil (FO)~~ for up to 8 weeks and then exposed acutely to DON by oral gavage. DON-induced plasma IL-6 and splenic mRNA elevation in FO-fed mice were significantly suppressed after 8 weeks when compared to the CO-fed group. The effects of FO on phosphorylation of mitogen-activated protein kinases (MAPKs), critical upstream transducers of IL-6 up-regulation, were also assessed. DON-induced phosphorylation of extracellular signal regulated protein kinases 1 and 2 (ERK1/2) and c-Jun N-terminal kinases 1 and 2 (JNK1/2) was significantly suppressed in spleens of mice fed with FO, whereas p38 was not. Splenic COX-2 mRNA expression, which has been previously shown to enhance DON-induced IL-6, was also significantly decreased by FO, whereas plasma levels of the COX-2 metabolite, prostaglandin E-2, were not affected. To confirm in vivo findings, the effects of pretreatment with the two primary n-3 PUFAs in FO, eicosapentaenoic acid (20:5[n-3]; EPA) and docosahexaenoic acid, (22:6[n-3]; DHA), on DON-induced IL-6 expression were assessed in LPS-treated RAW 264.7 macrophage cells. Consistent with the in vivo findings, both EPA and DHA significantly suppressed IL-6 superinduction by DON, as well as impaired DON-induced ERK1/2 and JNK1/2 phosphorylation. In contrast, the n-6 PUFA arachidonic acid (20:4[n-3]) had markedly less effects on these MAPKs. Taken together, the capacity of FO and its component n-3 PUFAs to suppress IL-6 expression as well as ERK 1/2 and JNK 1/2 activation might explain, in part, the reported suppressive effects of these lipids on DON-induced IgA nephropathy. (C) 2003 Elsevier Inc. All rights reserved.

L9 ANSWER 18 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:365843 SCISEARCH
THE GENUINE ARTICLE: 668RX
TITLE: Deoxynivalenol-induced IgA production and IgA nephropathy-aberrant mucosal immune response with systemic repercussions
AUTHOR: Pestka J J (Reprint)
CORPORATE SOURCE: Michigan State Univ, Inst Environm Toxicol, Dept Food Sci & Human Nutr, Dept Microbiol & Mol Genet, 234 GM Trout Food Sci & Human Nutr Bldg, E Lansing, MI 48824 USA (Reprint); Michigan State Univ, Inst Environm Toxicol, Dept Food Sci & Human Nutr, Dept Microbiol & Mol Genet, E Lansing, MI 48824 USA
COUNTRY OF AUTHOR: USA
SOURCE: TOXICOLOGY LETTERS, (11 APR 2003) Vol. 140, Sp. iss. SI, pp. 287-295.
Publisher: ELSEVIER SCI IRELAND LTD, CUSTOMER RELATIONS

MANAGER, BAY 15, SHANNON INDUSTRIAL ESTATE CO, CLARE,
IRELAND.

ISSN: 0378-4274.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 63

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Dietary exposure to the common foodborne mycotoxin deoxynivalenol (DON) selectively upregulates serum immunoglobulin A (IgA) in the mouse, most of which is polymeric, thus suggesting that the mucosal immune system is a primary target. When ingested, DON has no adjuvant or antigen properties but, rather, induces polyclonal IgA synthesis and serum elevation in an isotype-specific fashion. Resultant hyperelevated IgA is polyspecific, autoreactive and is likely to be involved in immune complex formation as well as kidney mesangial deposition. These latter effects mimic IgA nephropathy, the most common human glomerulonephritis. At the cellular level, DON upregulates production of T helper cytokines and enhances T cell help for IgA secretion. Analogous effects are observed in the macrophage with IL-6 being of particular importance based on ex vivo reconstitution and antibody ablation studies as well as experiments with IL-6 deficient mice. Upregulation of cytokines by DON involves both increased transcriptional activation and mRNA stability which are mediated by activation of mitogen-activated protein kinases. Interestingly, dietary omega-3 fatty acids can downregulate these processes and ameliorate DON-induced IgA nephropathy. From the perspective of gut mucosal immunotoxicology, these studies demonstrate that the capacity of a chemical to affect mucosal immune response can have systemic repercussions and, further, that these effects can be modulated by an appropriate nutritional intervention. (C) 2003 Elsevier Science Ireland Ltd. All rights reserved.

L9 ANSWER 19 OF 20--SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on
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ACCESSION NUMBER: 1999:729862 SCISEARCH

THE GENUINE ARTICLE: 237TB

TITLE: Fusarium mycotoxins: a review of global implications for animal health, welfare and productivity

AUTHOR: DMello J P F (Reprint); Placinta C M; Macdonald A M C

CORPORATE SOURCE: SCOTTISH AGR COLL, DEPT BIOTECHNOL, W MAINS RD, EDINBURGH EH9 3JG, MIDLOTHIAN, SCOTLAND (Reprint).

COUNTRY OF AUTHOR: SCOTLAND

SOURCE: ANIMAL FEED SCIENCE AND TECHNOLOGY, (30 AUG 1999) Vol. 80, No. 3-4, pp. 183-205.

Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.

ISSN: 0377-8401.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: AGR1

LANGUAGE: English

REFERENCE COUNT: 93

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Trichothecenes, zearalenone (ZEN) and fumonisins are the major Fusarium mycotoxins occurring on a worldwide basis in cereal grains, animal feeds and forages. Other important Fusarium mycotoxins include moniliformin and fusaric acid. Spontaneous outbreaks of Fusarium mycotoxicoses have been recorded in Europe, Asia, New Zealand and South America and, in addition, chronic exposure occurs on a regular and more widespread scale. The metabolism and adverse effects of the Fusarium mycotoxins are considered in this review with particular reference to recent data on specific and proposed syndromes and to interactions among co-occurring mycotoxins. Within the trichothecene group, deoxynivalenol (DON) is associated with emesis, feed refusal and depressed feed intake in pigs,

while T-2 toxin and diacetoxyscirpenol (DAS) are now clearly linked with oral lesions in poultry. The gut microflora of farm livestock are able to transform DON to a de-epoxy derivative. In contrast, the ovine metabolism of ZEN results in the production of five metabolites and relatively high levels of these forms may be excreted in the urine as glucuronides. There is now undisputed evidence that ZEN and its metabolites possess estrogenic activity in pigs, cattle and sheep, but T-2 toxin has also been implicated in reproductive disorders in farm livestock. Fumonisin is positively linked with pulmonary edema in pigs, leukoencephalomalacia in equines and with deranged sphingolipid metabolism in these animals. Fusarium mycotoxins have also been provisionally implicated in ovine ill-thrift, acute mortality of poultry and in duodenitis/proximal jejunitis of horses. Several Fusarium mycotoxins may co-occur in a particular feed ingredient or in compound feedingstuffs. In general, combinations of Fusarium mycotoxins result in additive effects, but synergistic and/or potentiating interactions have been observed and are of greater concern in livestock health and productivity. Synergistic effects have been reported between DON and fusaric acid; DON and fumonisin B-1 (FB1); and DAS and the Aspergillus-derived aflatoxins. Limited evidence of potentiation between FB1 and DON or T-2 toxin has also emerged recently. Additive and synergistic effects between known and unidentified mycotoxins may account for enhanced adverse effects observed on feeding Fusarium-contaminated diets. The potential for transmission of DON into eggs and of ZEN into porcine kidney and liver has been demonstrated. However, lactational carry-over of FB1 appears not to occur, at least in cows and sows. It is concluded that livestock health, welfare and productivity may be severely compromised by consumption of DON, T-2 toxin, DAS, ZEN and fumonisins and by interactions among these mycotoxins. Safety of some animal products may also be at risk. Furthermore, in view of the limited options available for remediation, it is concluded that exploitation of crops resistant to Fusarium infection offers the most viable strategy for reducing mycotoxin contamination of grain and animal feed. (C) 1999 Elsevier Science B.V. All rights reserved.

L9 ANSWER 20 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 97:741663 SCISEARCH
 THE GENUINE ARTICLE: XZ071
 TITLE: Transformation of nivalenol by gastrointestinal microbes
 AUTHOR: Hedman R (Reprint); Pettersson H
 CORPORATE SOURCE: SWEDISH UNIV AGR SCI, DEPT ANIM NUTR & MANAGEMENT, POB 7024, S-75007 UPPSALA, SWEDEN (Reprint)
 COUNTRY OF AUTHOR: SWEDEN
 SOURCE: ARCHIVES OF ANIMAL NUTRITION-ARCHIV FUR TIERERNAHUNG, (15 AUG 1997) Vol. 50, No. 4, pp. 321-329.
 Publisher: HARWOOD ACAD PUBL GMBH, C/O STBS LTD, PO BOX 90, READING, BERKS, ENGLAND RG1 8JL.
 ISSN: 0003-942X.
 DOCUMENT TYPE: Article; Journal
 FILE SEGMENT: AGRI
 LANGUAGE: English
 REFERENCE COUNT: 29

ABSTRACT IS AVAILABLE IN THE ALL AND ALL FORMATS

AB The capacity of the gastrointestinal microflora of pig, cow, and chicken to metabolize nivalenol (NIV) and deoxynivalenol (DON) was studied both in vivo and in vitro. Before feeding NIV to pigs, no metabolites of NIV or DON were formed in anaerobic incubates of the toxins with the pigs feces. However, after one week on a diet containing 2.5 or 5 ppm NN, nearly all excreted NIV in feces had been de-epoxidated in five of six pigs. After three weeks on the NIV diet also the sixth pig had acquired this ability. Deoxynivalenol was also de-epoxidated when incubated in vitro with the microorganisms

that formed de-epoxy-NIV in vivo. Anaerobic incubation of NIV and DON with cow rumen fluid produced de-epoxides of both toxins in a high proportion. No de-epoxide of NIV, but another unidentified metabolite was found in feces from chicken fed 2.5 or 5 ppm NIV for three weeks.